REMARKS

1. Interview of 1 September 2005

The helpfulness and courtesies of the Examiners during the interview of 1 September 2005 are appreciated. The discussions during the interview focused mainly on the relationship of the claims to the cited prior art to Schenk. Applicant's representative explained that the prior art does not teach insertion of a T helper epitope into an autologous sequence.

During the interview, the Examiners suggested that Applicants consider amending the claims to better clarify the "insertion" of the T helper epitopes into the autologous sequences. This distinction is further discussed below.

In addition, the Examiners suggested that the claims might be amended to include some "functional" language to require that the antibodies produced by the claimed method are antibodies against the autologous Aβ or autologous APP. But the Examiners will note that each of the independent claims already include a "whereby clause" that recites this feature by stating that "whereby administration to said mammal with said modified Aβ or APP polypeptide induces production of antibodies against the autologous Aβ or autologous APP polypeptide in said mammal". Applicants suggest that this already existing language satisfies the Examiners' request.

2. Amendments to the Claims

As noted above, the independent claims have been amended to better clarify the means by which the T helper epitopes are introduced into the autologous Aβ and APP polypeptide sequences. It is possible, according to the present invention, to introduce at T helper epitope by either inserting an isolated epitope into the autologous sequence, or by substitution/replacement of amino acids in the autologous sequence to thereby result in the creation of a T helper epitope. Claims 1 and 76 have been amended to better clarify these two aspects of the invention and those claims are generic to both aspects. Claims 7, 71 and 74 specifically recite that at least one T helper epitope is inserted into the autologous sequence; whereas, claim 19 recites that a T helper epitope is created by substitution of at least one amino acid in the autologous sequence.

Claims 81 – 83 have been added to the application and are directed to specific embodiments described in the specification as follows:

Claim 81 is directed to construct 34 in the table on page 85 of the specification.

Claim 82 is directed to construct 2 in the table on page 85 of the specification.

Claim 83 is directed to construct 3 in the table on page 85 of the specification.

3. Claim Objections

The Examiner has objected to some of the claims as being substantial duplicates of other claims. Applicants submit that the claims are not duplicates for the following reasons.

Claim 71 is directed to a method comprised of administering a modified polypeptide; whereas, claim 1 is more broadly directed to "effecting presentation". A similar distinction differentiates claims 76 and 74.

Claims 78/77 and 80/79 are different because they depend on different independent claims, which themselves are distinguished for the above reasons.

4. Double Patenting Rejection

The claims have been rejected for obviousness-type double patenting over claims 1-22 of co-pending application no. 10/204,362, and for obviousness- type double patenting claims 1-21 of co-pending application no. 10/223,809. Applicants wish to defer action on these objections until such time as the claims are indicated as being allowable in the present application, particularly since the rejections are "provisional" obviousness-type double patenting rejections.

5. Rejections Under 35 USC 102(e)

The claims have been rejected under 35 USC 102(e) as being anticipated by Schenk '637 or Schenk '523. These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

5.1. Rejection over Schenk '637

As noted above, during the interview, Applicant's representative urged that none of the prior art teaches the insertion of a T helper epitope into an autologous Aβ or autologous APP polypeptide. Schenk teaches that "a peptide immunogen can be linked to a suitable carrier to help elicit an immune response" (see column 20, lines 22 – 23 of Schenk '627), but this is far different from the present invention as pictorially shown in attached Exhibit 1, a copy of which was provided to the Examiner during the interview. To better clarify this distinction, the independent claims have been amended to focus on the insertion of the T helper epitope into the autologous Aβ or autologous APP polypeptide.

In making the prior art rejections the Examiner has relied on parts of the Schenk '637 patent that are not prior art to the present application. As previously explained, the Schenk '637 patent granted from an application which itself was a continuation-in-part of prior application serial no. 09/322,289 which was filed on May 28, 1999. Thus, only subject matter in the Schenk patent which is common to both the continuation application and the parent application could be prior art to the present application as of May 28, 1999. Material added into the Schenk et al. application upon the filing of the continuation-in-part application on May 26, 2000 would **not be prior art** to the present application because that date is after the priority date of the present application based upon Danish priority application PA 2000 00265 and the priority provisional application 60/186,295 filed on March 1, 2000.

The key difference to note is that the discussion in the Schenk '637 patent at column 20, lines 28 – 51 relating to T-cell epitopes is **completely missing** from the corresponding portion (page 24, line 9) of the earliest Schenk application. For the Examiner's easy understanding, a copy of the relevant pages of the Schenk '637 patent and earliest application are enclosed with the differences being noted (see Exhibits 2 and 3). Again, a copy of these pages was shown to the Examiner during the interview.

The Schenk '637 patent includes a section entitled "Carrier Proteins" (column 20) which describes that "a peptide immunogen can be linked to a suitable carrier to help elicit an immune response." But the present invention is still different from Schenk, because Schenk only describes one of the following three types of constructs:

(a) a carrier protein is linked to the immunogen; whereas the present invention teaches linkage of the immunogen to isolated T-helper epitopes;

(b) the immunogen may be placed internally in the carrier protein; whereas the present invention is essentially the "inverse", namely placement of a T-helper epitope inside the immunogen; and

(c) use of "multiple repeats of the immunogen", but Schenk does not indicate how these multiple repeats appear in the immunogen, so it does not suggest, for example, the presently claimed 3 or 9 Aβ copies where each copy is separated from the adjacent copy by a T-helper epitope. In addition, this aspect of Schenk still merely teaches coupling to carrier proteins, not insertion of a T-helper epitope inside of the immunogen.

Applicants submit that the Examiner, therefore, has not properly analyzed the true disclosure of the Schenk patent that is prior art to the present application. The rejection should, therefore, alone be withdrawn.

5.2. Rejection over Schenk '523

As with Schenk '687, the Schenk '523 patent also fails to teach the insertion of a T helper epitope into an autologous Aβ or autologous APP polypeptide as claimed in the present invention. In making the rejection, the Examiner asserts that the two Schenk patents teach the same features, though they may differ in the particular cited column, line or other page number. So as with Schenk '687, the Schenk '523 patent teaches that a peptide immunogen can be linked to a suitable carrier to help elicit an immune response, but this is far different from the present invention as pictorially shown in attached Exhibit 1.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's rejections have been addressed and overcome, so that the claims now define patentable subject matter. Therefore, reconsideration and withdrawal of all of the rejections, and early allowance of all the claims are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the

telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicant petitioned for an extension of three months to February 8, 2006 for the period in which to file a response to the Office Action dated August 8, 2005 in the concurrently filed Notice of Appeal. The required fee has been paid in connection with the proper filing of this Notice of Appeal.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
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LRS/lmt
4614-0112P

Attachment(s)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on: February 7, 2006
(Date of Deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Lori M. Hill
(Signature)

February 7, 2006
(Date of Signature)

EXHIBIT 1

INVENTION

Claim 1

 Autologous Amyloid Beta or ABB protein.

- T helper EPITOPES: tetanus toxoid, diphtheria toxoid, P. falciparum CS epitope, influenza HA epitope, and MHCII T cell binding peptide.

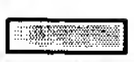
Claim 3

 Autologous Amyloid Beta or APP protein.

- T helper epitopes.
- Cytokines, etc.

Claim 77 = multimers of the fusion protein of the invention.

SCHENK APPLICATION

 Amyloid Beta or APP protein.

 Carrier PROTEIN, *eg* toxoid PROTEIN, diphtheria toxoid PROTEIN, etc.

Multimers of the above.

SCHENK PATENT

Introduces "epitope" / MHCII binding peptide.

EXHIBIT 3

P1 271656

3

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

July 11, 2000

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE UNDER 35 USC 111.

APPLICATION NUMBER: *09/322,289*
FILING DATE: *May 28, 1999*
PCT APPLICATION NUMBER: *PCT/US00/14810*

By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS

S. Woodson
N. WOODSON
Certifying Officer

PRIORITY DOCUMENT

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ASSISTANT COMMISSIONER FOR PATENTS
BOX PATENT APPLICATION
Washington, D.C. 20231

Attorney Docket No. 15270-004740US

"Express Mail" Label No. EM035146624US

Date of Deposit: May 28, 1999

I hereby certify that this is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above, addressed to:

Assistant Commissioner for Patents
Washington, D.C. 20231

By: J. Liebeschuetz

Sir:
Transmitted herewith for filing under 37 CFR 1.53(b) is the
[X] patent application of
[ ] continuation patent application of
[ ] divisional patent application of
[ ] continuation-in-part patent application of

Inventor(s)/Applicant Identifier: Dale B. Schenk

For: PREVENTION AND TREATMENT OF AMYLOIDOGENIC DISEASE

[ ] This application claims priority from each of the following Application Nos./filing dates: _____ the disclosures of which are incorporated by reference.

[ ] Please amend this application by adding the following before the first sentence: "This application is a [ ] continuation [ ] continuation-in-part of and claims the benefit of U.S. Application No. 60/_____, filed _____, the disclosure of which is incorporated by reference."

Enclosed are:
[X] 88 pages of specification
[X] 5 pages of claims
[X] 1 page of Abstract
[X] 16 sheets of drawings
[X] Unsigned Declaration and Power of Attorney
[X] Return Postcard.

In view of the Unsigned Declaration as filed with this application and pursuant to 37 CFR §1.53(f), Applicant requests deferral of the filing fee until submission of the Missing Parts of Application.

DO NOT CHARGE THE FILING FEE AT THIS TIME.

J. Liebeschuetz

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PA 195224 v1

Attorney Docket No.: 15270-47-4
Client Reference No.: 00209-US-CIP4

PATENT APPLICATION

PREVENTION AND TREATMENT OF AMYLOIDOGENIC DISEASE

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PATENT
Attorney Docket No.: 15270-47-4
Client Reference No.: 00209-US-CIP4

PREVENTION AND TREATMENT OF AMYLOIDOGENIC DISEASE

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is related to USSN 60/067,740, filed December 2, 1997, USSN 60/080,970, filed April 7, 1998, and USSN 09/201,430, filed November 30, 1998, each of which is incorporated by reference in its entirety for all purposes.

TECHNICAL FIELD

The invention resides in the technical fields of immunology and medicine.

BACKGROUND OF THE INVENTION

Alzheimer's disease (AD) is a progressive disease resulting in senile dementia. *See generally* Selkoe, *TINS* 16, 403-409 (1993); Hardy et al., WO 92/13069; Selkoe, *J. Neuropathol. Exp. Neurol.* 53, 438-447 (1994); Duff et al., *Nature* 373, 476-477 (1995); Games et al., *Nature* 373, 523 (1995). Broadly speaking the disease falls into two categories: late onset, which occurs in old age (65 + years) and early onset, which develops well before the senile period, i.e, between 35 and 60 years. In both types of disease, the pathology is the same but the abnormalities tend to be more severe and widespread in cases beginning at an earlier age. The disease is characterized by at least two types of lesions in the brain, senile plaques and neurofibrillary tangles. Senile plaques are areas of disorganized neuropil up to 150 μm across with extracellular amyloid deposits at the center visible by microscopic analysis of sections of brain tissue. Neurofibrillary tangles are intracellular deposits of microtubule associated tau protein consisting of two filaments twisted about each other in pairs.

The principal constituent of the plaques is a peptide termed Aβ or β-amyloid peptide. Aβ peptide is an internal fragment of 39-43 amino acids of a precursor protein termed amyloid precursor protein (APP). Several mutations within the APP protein have been correlated with the presence of Alzheimer's disease. See, e.g., Goate et al., *Nature* 349, 704) (1991) (valine^{717} to isoleucine); Chartier Harlan et al. *Nature* 353, 844 (1991)) (valine^{717} to glycine); Murrell et al., *Science* 254, 97 (1991) (valine^{717} to phenylalanine); Mullan et al., *Nature Genet.* 1, 345 (1992) (a double mutation changing lysine^{595}-methionine^{596} to asparagine^{595}-leucine^{596}). Such mutations are thought to cause

1. Carrier Proteins

Some agents for inducing an immune response contain the appropriate epitope for inducing an immune response against amyloid deposits but are too small to be immunogenic. In this situation, a peptide immunogen can be linked to a suitable carrier to help elicit an immune response. Suitable carriers include serum albumins, keyhole limpet hemocyanin, immunoglobulin molecules, thyroglobulin, ovalbumin, tetanus toxoid, or a toxoid from other pathogenic bacteria, such as diphtheria, E. coli, cholera, or H. pylori, or an attenuated toxin derivative. Other carriers for stimulating or enhancing an immune response include cytokines such as IL-1, IL-1 α and β peptides, IL-2, ΓINF, IL-10, GM-CSF, and chemokines, such as MIP1α and β and RANTES. Immunogenic agents can also be linked to peptides that enhance transport across tissues, as described in O'Mahony, WO 97/17613 and WO 97/17614.

Immunogenic agents can be linked to carriers by chemical crosslinking. Techniques for linking an immunogen to a carrier include the formation of disulfide linkages using N-succinimidyl-3-(2-pyridyl-thio) propionate (SPDP) and succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC) (if the peptide lacks a sulfhydryl group, this can be provided by addition of a cysteine residue). These reagents create a disulfide linkage between themselves and peptide cysteine resides on one protein and an amide linkage through the å-amino on a lysine, or other free amino group in other amino acids. A variety of such disulfide/amide-forming agents are described by *Immun. Rev.* 62, 185 (1982). Other bifunctional coupling agents form a thioether rather than a disulfide linkage. Many of these thio-ether-forming agents are commercially available and include reactive esters of 6-maleimidocaproic acid, 2-bromoacetic acid, and 2-iodoacetic acid, 4-(N-maleimido-methyl)cyclohexane-1-carboxylic acid. The carboxyl groups can be activated by combining them with succinimide or 1-hydroxyl-2-nitro-4-sulfonic acid, sodium salt.

Immunogenic peptides can also be expressed as fusion proteins with carriers. The immunogenic peptide can be linked at the amino terminus, the carboxyl terminus, or internally to the carrier. Optionally, multiple repeats of the immunogenic peptide can be present in the fusion protein.

The same or similar carrier proteins and methods of linkage can be used for generating immunogens to be used in generation of antibodies against Aβ for use in

* Does not contain description found at col. 20, lines 28-51 of U.S. Pat. 6,787,637 B1